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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,631	07/28/2003	Marc Achen	28967/56801D	3314

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MARSHALL, GERSTEIN & BORUN LLP
233 S. WACKER DRIVE, SUITE 6300
SEARS TOWER
CHICAGO, IL 60606

EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
11/13/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/627,631	ACHEN ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-13,41 and 45-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13, 41, and 45-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 10-13, 41, and 45-50 are pending.

2. The typographical error "WO 98/33485" at page 5 of the amendment filed July 28, 2008 should have been WO 99/33485.

3. The rejection of claims 9-13, 41 and 45-47 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps has been obviated by the claims amendment filed July 28, 2008.

4. The rejection of claims 9-13, 41 and 45-47 under 35 U.S.C. 102(b) as being anticipated by WO 99/33485 publication (of record, published July 8, 1999, PTO 1449) has been obviated by the claims amendment filed July 28, 2008.

5. The new matter rejection of claims 9-13, 41 and 45-47 under 35 U.S.C. 112, first paragraph has been obviated by the claims amendment filed July 28, 2008.

6. The following new ground of rejection is necessitated by the amendment filed July 28, 2008.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was

made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 10-13, 41 and 45-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/33485 publication (of record, published July 8, 1999; PTO 1449) in view of Kurebayashi et al (Jpn J Cancer Res 90: 977-981, Sept 1999; PTO 892).

The WO 99/33485 publication teaches a method of diagnosing neoplastic disease such as human malignant melanoma as an indicator of future metastatic risk (see page 20, line 11-12, in particular). The reference method comprises contacting a cancer biopsy specimens or tissue sample from an organism such as human or biological sample expressing VEGF-D with a specific binding reagent such as monoclonal antibody that binds to VEGF-D (see page 20, lines 1-8, Figure 7, in particular), measuring the amount of VEGF-D polypeptide in the sample which will be useful as an indicator of future metastatic risk (see page 20, lines 9-10, in particular). The WO 99/33485 publication teaches various monoclonal antibodies such as 4A5; the reference 4A5 antibody was later renamed as VD I as evidenced in page 48 of instant specification that binds specifically to unprocessed (full-length) VEGF-D) for immunohistochemistry analysis (See page 32, lines 18-19, in particular). The WO 99/33485 publication further teaches unprocessed VEGF-D has a molecular weight of approximately 53 KDa (see page 40, lines 3-6, Figure 9A-C, in particular). The reference unprocessed VEGF-D, also known as full-length VEGF-D, activates VEGFR-3 but not VEGFR-2 (see page 19, line 21-22, page 45, lines 15-16, in particular) and VEGFR-3 is expressed on lymphatic endothelial cells of the lymphatic vessels in the vicinity of the tumor (See paragraph bridging page 35 and 36, in particular). The reference antibody may covalently or non-covalently coupled to a label such as supermagnetic, paramagnetic, or radioactive agent such as 125I or 32P, or non-radioactive labels such as Streptavidin-alkaline phosphatase, enzyme label such as horseradish peroxidase, or fluorimetric labels such as fluorescein-5-isothiocyanate (FITC) for imaging or for diagnostic purposes (see page 20, lines 11-21, page 33, claim 30 of the WO 99/33485, in particular). The reference sample comprises endothelial cells (see page 34, lines 8-25, Figure 7A-C, in particular). WO 99/33485 publication teaches VEGF-D monoclonal antibodies (MAbs) detected VEGF-D in melanoma tumor cells, in addition to endothelial cells of blood vessels in the vicinity of the tumor cells producing VEGF-D (see page 35, line 13-24, in particular). The increase amount of VEGF-D is evidenced by the more pronounced staining in small islands of tumor cells at the periphery of the invasive portion

of the tumor, which correlates with increased tumor growth or metastatic risk (see page 34, lines 8-15, Figure 7A-B, in particular). Claim 41 is included in this rejection because the WO 99/33485 publication teaches breast cancer associated with lymph node metastasis and obstruction; increasing amount of the VEGF-D induces lymphangiogenesis (see page 17, line 11-17, in particular).

The invention differs from the teachings of the reference only in that measuring amount of unprocessed VEGF-D polypeptide having a molecular weight of approximately 53 K in the sample and wherein the increased unprocessed VEGF-D having a molecular weight of approximately 53K in said sample correlates with increased tumor growth or metastatic risk.

Kurebayashi et al teach VEGF-D is expressed in the lymph node-positive tumors from human breast cancer specimens and not from node-negative tumors (see page 980, left col. first paragraph, page 979, Table III, in particular). Further, VEGF-D expression was detected in an inflammatory breast cancer and such tumor which developed an inflammatory skin metastasis (see abstract, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to detect VEGF-D in any sample comprising a lymph node from patient with breast ductal carcinoma as taught by Kurebayashi et al using the anti-VEGF-D antibody as taught by the WO 99/33485 publication.

One having ordinary skill in the art would have been motivated with the expectation of success to detect VEGF-D in any sample obtained from patient with malignant disease because Kurebayashi et al teach VEGF-D is associated with metastatic risk since VEGF-D detection in inflammatory breast cancer, which later developed an inflammatory skin metastasis (see abstract, in particular).

One having ordinary skill in the art would have been motivated the expectation of success to detect VEGF-D in any sample obtained from patient with malignant disease because the WO 99/33485 publication teaches increasing amount of VEGF-D is evidenced by the more pronounced staining in small islands of tumor cells at the periphery of the invasive portion of the tumor, which correlates with increased tumor growth or metastatic risk (see page 34, lines 8-15, Figure 7A-B, in particular).

It is within the purview of one of ordinary skill in the art at the time the invention was made to recognize that the use of the reference antibody 4A5 antibody, which is the same antibody used by applicants as evidenced by page 48 of instant application, would obviously

detect the same unprocessed VEGF-D having a molecular weight of approximately 53 KDa as taught by the WO 99/33485 publication (see page 40, lines 3-6, Figure 9A-C, in particular). Given the teachings of the references, one having ordinary skill in the art at time the invention was made would have been expected that an increase in VEGF-D in any sample correlates with increased tumor metastatic risk because VEGF-D is detected in metastatic lymph node-positive tumors from human breast cancer specimens but not from non-metastatic node-negative tumor as taught by Kurebayashi et al.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O'Hara can be reached on (571) 272-0878. The IFW official Fax number is (571) 273-8300.

13. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
November 7, 2008